GE Healthcare
Life Sciences

Xuri™ Cell Expansion System W25

The single-use Xuri Cell Expansion System W25 is a reliable and intuitive cell expansion device for working volumes up to 25 l (Fig 1). The system is based on the well-known WAVE™ rocking technology that provides mixing and aeration to the culture. With the Xuri Cell Expansion System W25 , the rocking is enhanced with features such as advanced sensors and intelligent control strategies. System operation is easily managed via the intuitive and user friendly UNICORN™ system control software. The system is designed for fast installation and convenient handling, and delivers a reliable and accurate performance suitable for research, process development, and manufacturing operations.

Fig 1. Xuri Cell Expansion System W25 bioreactor system.

Xuri Cell Expansion System W25 offers the following benefits:

- Minimize the risk of cell contamination with a functionally closed system
- Reach high cell densities with confidence
- Be in charge of your cell expansion with process monitoring and remote control
- Designed for use in a regulated environment

Applications

Xuri Cell Expansion System W25 is intended for a variety of cell culture applications incuding:

- Rapid production of clinical grade T-lymphocytes
- Perfusion culture of T-lymphocytes
- Perfusion culture of human natural killer cells

System benefits

Minimize the risk of cell contamination with a functionally closed system

The Xuri Cell Expansion System W25 is a single-use, functionally closed system meaning that the chance of contamination between different patient samples or with adventitious agents is minimized.

Reach high cell densities with confidence

Perfusion is easy on the Xuri Cell Expansion System W25. Perfusion allows high cell densities to be obtained in the Cellbag. This means that an entire therapeutic dose can be obtained in one closed bioreactor system, eliminating the difficulties with combining culture vessels as is required with manual systems. High cell density and reduced manufacturing footprint allows you to maximize use of your limited manufacturing space.

Be in charge of your cell expansion with process monitoring and remote control

The Xuri Cell Expansion System W25 is designed to put complete control of the culture in your hands whether you are standing next to the bioreactor or at home in the evening. By giving you control of process parameters such as rocking speed, DO, pH and perfusion rate, you can optimize your cell culture protocol to obtain therapeutic cells in the most efficient manner for you. Once the culture is setup, remote monitoring gives you the peace of mind to leave it knowing that you will be alerted if anything changes from the limits you set.

Lid
Graphical user interface
Xuri Cell Expansion W25 Pump
Peristaltic pump
Client computer
Installed with UNICORN software
Tray
Xuri Cell Expansion System W25 Base Unit
Rocker, temperature sensors, scale, embedded controller, and dual hard drives
Xuri Cell Expansion W25 Environmental Control Unit
Gas flow/mix controller, pH, and DO sensors

System setup and integration of subunits

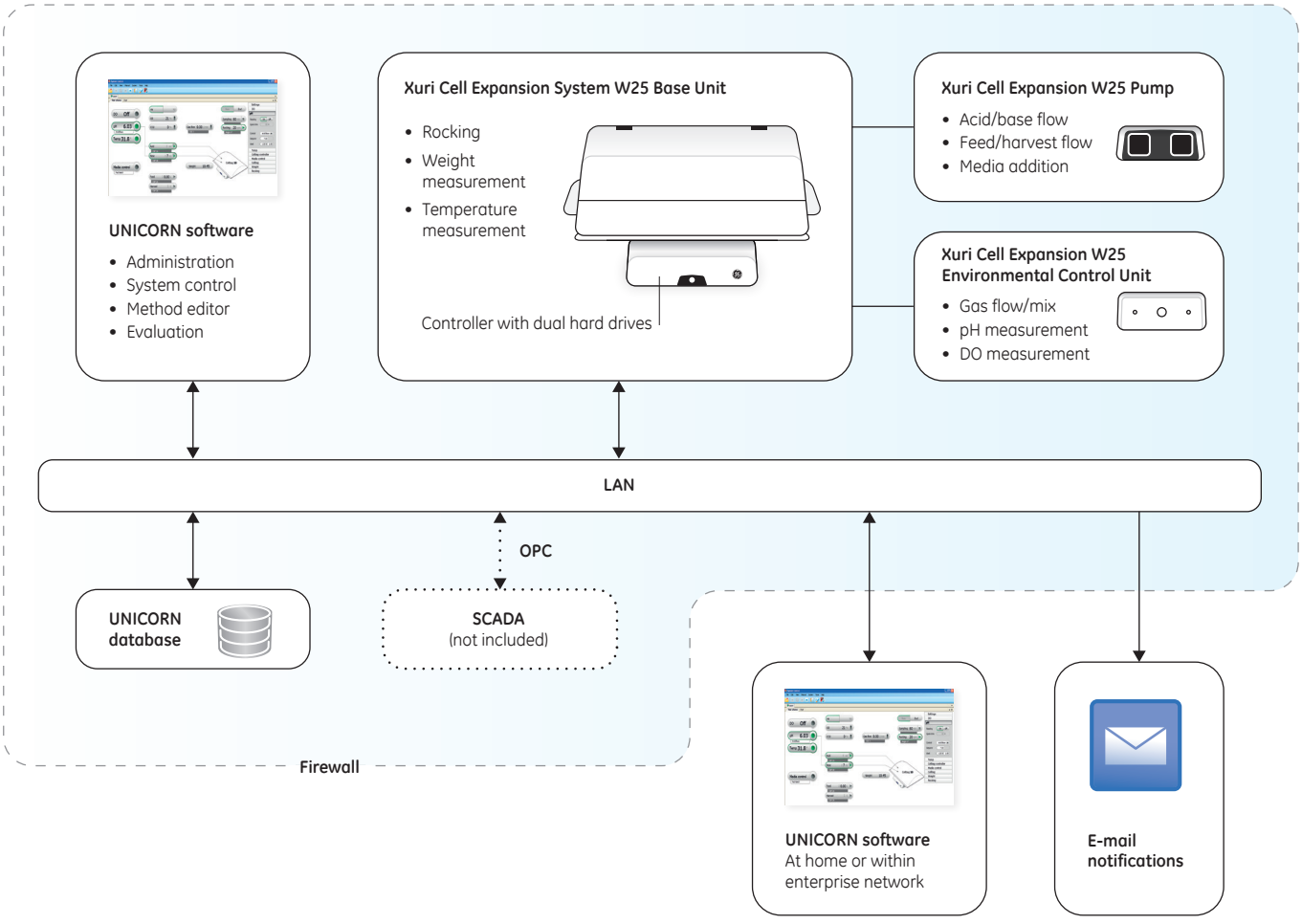

Fig 2. Xuri Cell Expansion System W25 overview. The System Control module on the client computer is used to start and monitor the cultivation process. One UNICORN client can control up to three Xuri Cell Expansion W25 systems simultaneously. SCADA = supervisory control and data acquisition, OPC = open platform communications, LAN = local area network.

Designed for use in a regulated environment

The Xuri Cell Expansion System W25 is designed to meet the demands and standards that are required in a regulated environment. The documentation is extensive and includes material certificates, system specifications, installation and operational qualification (IQ/OQ) protocols, and a detailed user manual. The UNICORN software is suitable for use in a manner that complies with 21 CFR Part 11 and Good Automated Manufacturing Practice (GAMP) 5.

System overview

Xuri Cell Expansion System W25 components

The Xuri Cell Expansion System W25 consists of a base unit, a gas mixer, and a pump, all operated by the UNICORN software installed on a client computer. The base unit is the main unit and is used together with a tray and a disposable Cellbag bioreactor. The base unit has multiple functions, amongst them heating, culture mixing, and weight measurement. The gas mixer delivers gas of a defined composition to the culture and is used, together with the optical sensors of the Cellbag bioreactor, for online control of culture pH and DO. Liquid is delivered accurately to the culture by the Xuri Cell Expansion W25 pump. The pump unit has a flow range covering multiple applications, from additions of acid and base to fresh medium for perfusion culture. An overview of the Xuri Cell Expansion System W25 is shown in Figure 2. The individual components are described in detail below.

A)

B)

Fig 3. (A) Xuri Cell Expansion System W25 in tilt position. (B) The ergonomic design makes activities such as sampling and harvest convenient and easy.

Xuri Cell Expansion W5, base unit

The base unit is the main hardware unit of the system and provides mixing through the rocking, reliable temperature measurement from integrated sensors, and accurate weight measurement from integrated load cells. The ergonomic design makes handling convenient and easy. The ability to handle the bioreactor in a tilt position facilitates sampling and harvest (Fig 3). The minimal footprint facilitates placement when space is limited.

Trays and lids

Trays are available in three different sizes for culturing of up to 5 l, 10 l, and 25 l. The trays are easily attached to the base unit when in the tilt position. A snap lock mechanism allows Cellbag bioreactors to be correctly installed and rapidly changed (Fig 4). To protect light-sensitive components of the culture medium and to prolong the life of the optical sensors, lids are available for all tray sizes.

Fig 4. The tray has an easy lock mechanism for convenient and proper attachment of Cellbag bioreactors.

Temperature control

Reliable, efficient, and evenly distributed heating is provided by the tray heater plate. The temperature measurement is managed by sensors integrated in the rocker base unit (Fig 5). To minimize the risk for overheating, heating is only enabled when the base unit is in motion. For an accurate, stable, and fast temperature control, the heater power output is automatically adjusted based on the Cellbag bioreactor size and the media volume.

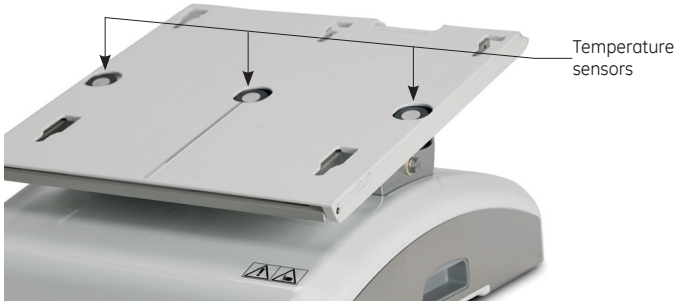

Fig 5. Integrated temperature sensors for convenient handling and reliable temperature control.

Mixing and gas transfer

The adjustable rocking parameters are speed, angle, and motion. The parameter settings, in combination with the cell culture volume, affect the mixing and gas transfer rate in the Cellbag bioreactor. The speed parameter determines the number of rocking cycles per minute, and the angle parameter relates to the tray's degree of tilting at the turning points. The motion parameter determines the acceleration profile. The lowest motion parameter setting, 15%, gives an almost constant speed throughout the rocking cycle, whereas the highest setting, 100%, gives a faster speed in the middle of the cycle and slower at the turning points (Fig 6). A lower percent setting will give a more aggressive mixing with higher gas transfer rates. A higher setting will result in a smoother wave suitable for more delicate applications, such as adherent cultivation on microcarriers.

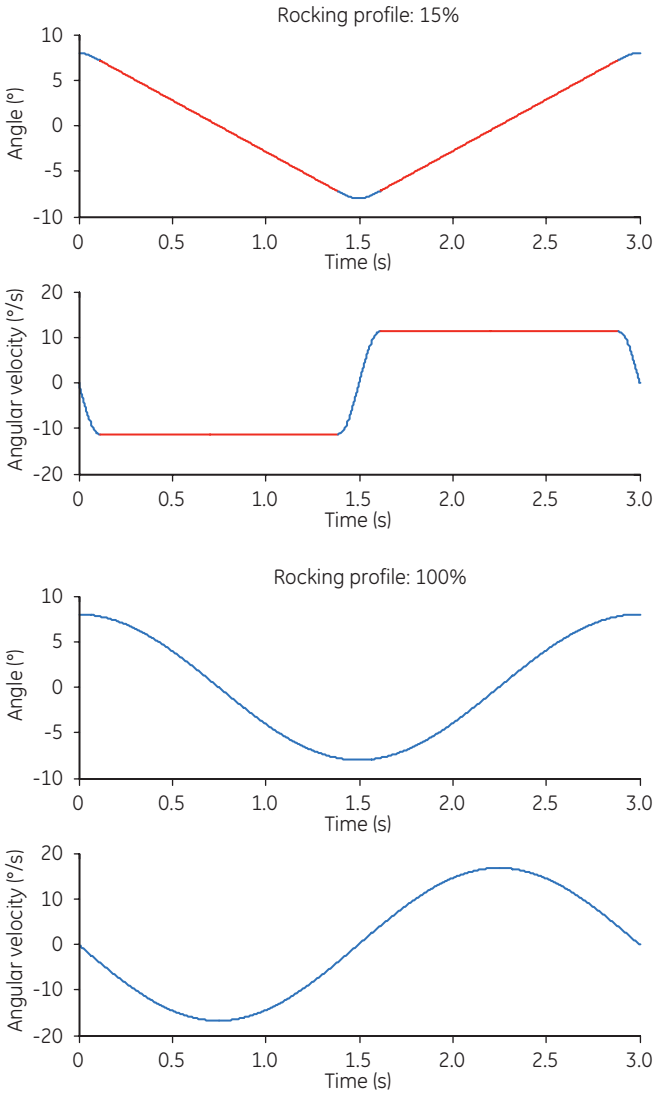

Fig 6. A user-defined rocking motion can be selected in UNICORN system control software. The wave can be aggressive or gentle, with subsequent impact on mixing and gas transfer in the culture.

Weight measurement

Load cells integrated in the base unit provide accurate and continuous weight measurement of the culture and eliminate the need for external scales. The load cells communicate with the system control function for proper media handling and for tailored regulation of pH and temperature. The weight measurement functionality is also used for automatic calibration of the pump in perfusion cultures. Adjustable feet enables equal weight distribution between the load cells also on non-level surfaces, for increased precision of the weight measurement.

Data storage and communication

All run data and control parameters are stored on two independent, mirrored solid state drives integrated in the base unit. Thus, once cultivation has been started and data from the instrument modules have been collected, the run can continue without the need for a network connection. The use of two solid state drives enables culturing without losing any data even if only one drive is functional. After a run, data is stored in a UNICORN database on an external computer. For facilitated integration into a larger manufacturing operation, the base unit also contains software for enabling direct communication with the system via an open platform communication (OPC) link.

Xuri Cell Expansion W25 Environmental Control Unit

Table 1. Environmental Control Unit overview

Feature	Description
CO_2/O_2/air mix controller	Depending on the configuration, air is mixed with CO_2 and/or O_2 according to the set-points. Nitrogen may be used instead of air for maintaining a low oxygen environment for near-anaerobic applications.
Gas flow controller	The gas-mix flow is measured and controlled by a mass flow controller (MFC). A correct volumetric flow is achieved by compensation for CO_2 concentration. Quick filling of gas into the Cellbag bioreactor, enabled by the fast-fill function, significantly reduces start-up time. An alarm will inform the user if pressure sensors detect under- or overpressure at the gas inlets or within the Cellbag bioreactor.
pH measurement	The pH is measured with optical pH sensors preinstalled in Cellbag bioreactors of pHOPT type. The sensor is connected to the Environmental Control Unit via an optical fiber cable.
DO measurement	The DO level is measured with optical DO sensors preinstalled in Cellbag bioreactors of DOOPT type. The sensor is connected to the Environmental Control Unit via an optical fiber cable.

The Xuri Cell Expansion W25 Environmental Control Unit is a compact unit with multiple functions. The unit is primarily

used for providing gas to the culture and for monitoring of pH and DO. The unit contains a controller for mass flow, sensors for gas pressure and O_2 and CO_2 concentrations, and transmitters for pH and DO (Table 1).

Two Environmental Control Unit configurations are available:

- CO_2, O_2, and pH
- CO_2, O_2, pH, and DO

The most suitable Environmental Control Unit configuration will depend on the specific application.

Xuri Cell Expansion W25 Pump

The Xuri Cell Expansion W25 pump is a peristaltic unit incorporating two roller pumps for feed, harvest, and pH control. The pump design makes tubing installation convenient and easy. Tubing sizes from 0.5 mm (1/50") to 4.8 mm (3/16") internal diameter can be used to support flow rates fom 0.07 to 100 ml/min. Flow rate is regulated by weight feedback from the scale and is controlled by automatic adjustments of the pump speed. Manual adjustment of the flow rate is also possible.

Media handling and perfusion using calibrated pumps

Calibration of pumps can be performed manually or automatically during an ongoing perfusion process. Automatic calibration is possible for flow rates above 3.5 l/d and is easily managed by entering the tubing diameter.

Automated pH control

To minimize fluctuations in pH during adjustments with CO_2/base or acid/base, the flow rate of the acid/base pumps needs to be rigorously monitored. The Xuri Cell Expansion System W25 uses combined information from the load cells, the current process pH value, the pump tubing diameter, and the acid/base molarity for calculation of the needed flow rate during the run.

UNICORN software

UNICORN system control software consists of four modules: ***Administration***, ***Method Editor, System Control***, and ***Evaluation***. A comprehensive help tool is also included.

Administration

The ***Administration*** module is used to administer all functions of the UNICORN software. Available functions include user and email setup, controlling access to groups and network users, defining and editing system properties, database management, and logging records of usage and activity.

Method editor

Instructions to control a bioreactor run can be defined in a method. The ***Method Editor*** module is used to create, edit, save, and work with methods. An existing method can be changed to simplify the editing process. Individual changes can be saved for later use on systems having the same instrument and component configuration.

System control

The ***System Control*** module is used to connect to the system as well as to start, view, and control a run (Fig 7). Default parameter values for an instrument can be viewed and edited in the ***System Settings*** dialog before a run is started or during an ongoing run using manual instructions. It is also possible to connect to other systems.

The user-friendly and intuitive ***Process Picture*** pane enables manual interaction with the system and provides status of the run parameters. Data is shown in the process picture but can also be viewed as curves in the ***Charts*** tab and as numerical values in the ***Run Data*** pane. Curves and information about the run are saved in a database, which can be opened in the ***Evaluation*** module. The default view shows the most commonly curves used. The user may customize which curves to display and the color and style of the displayed curves.

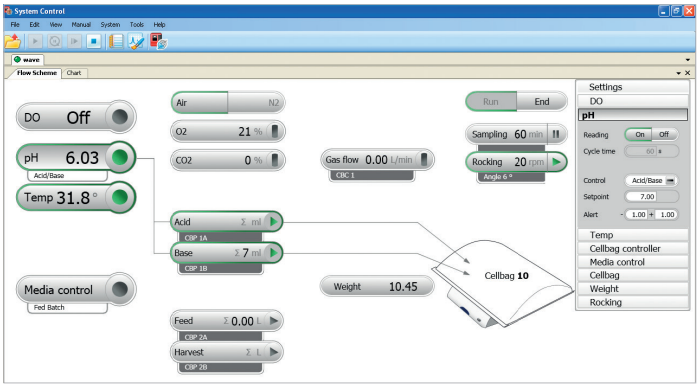

Fig 7. Monitoring and controlling all aspects of the culture is managed through the user-friendly interface.

Evaluation

In the ***Evaluation*** module, content of the result files can be viewed, analyzed, and compiled as reports. Reports can be customized, saved, and printed.

Automation of process parameters in pH and DO control

The UNICORN software automatically sets the desired PID* control parameters based on Cellbag bioreactor size and gas flow set-point. The system also adapts the parameters during the run, for optimization to reach a new set-point or to maintain a current set-point.

* Proportional-integral-derivative

Alarms, notifications, and data logging

The UNICORN software allows easy access to all operations, data, and alarm conditions. A dynamic, graphical user interface shows the real-time status of the run, while data are automatically saved. From the UNICORN software, the system is easily configured to trigger an alarm when certain conditions are met. Individual deviation alarms can be set for all essential

parameters (heating, gas flow, CO2, pH, and DO). Alarm sensitivity and delay is defined by the user. If such an alarm condition is triggered, the source of the alarm is highlighted in the graphical user interface and an alarm dialog is displayed. The alarm dialog displays information about the alarm, such as date and time of occurrence, as well as a help text describing the cause and how to solve the problem. The system is easily configued to send email notifications of alarms and errors

Regulatory readiness

The Xuri Cell Expansion System W25 is suitable for biomanufacturing of regulated products under various Quality Management Systems. The use of UNICORN software in a 21 CFR Part 11 and GAMP 5 compliant manner enables use of the system in a regulated environment. Individual user access permissions can be set and individual users are password-protected. Active processes can be locked to enable unattended operations without the risk of unauthorized interference. All records are stored in a single, unalterable database, including results and extended run documentation. Additional validation support includes comprehensive documentation on control system validation as well as IQ/OQ services. Available validation support documentation includes:

- Detailed description of the development model used for UNICORN software
- 21 CFR Part 11 system assessment in checklist format
- Audit report and 21 CFR Part 11 conclusion on functionality by an external, independent expert

Networking capabilities

UNICORN software operates in Windows XP® and Windows® 7 environments and the network ability allows real-time control from a remote or local computer. Communication is Ethernet-based and each instrument is controlled by a dedicated instrument server. One database can be connected to 32 systems and up to three instruments can be controlled simultaneously from one UNICORN client. Results are saved locally, in the base unit, during the run and then stored on the database server. Because results and instructions are saved locally on the embedded drives, a run can continue even in the event of a network communication failure.

UNICORN software can be integrated in a supervisory control and data acquisition (SCADA) system such as the Emerson DeltaV™ control system using the UNICORN OPC server.

Cellbag bioreactors

Cellbag bioreactors are single-use bags for the noninvasive mixing of culture medium and cells during cultivation (Fig 8). Cellbag bioreactors require no sterilization or cleaning steps. The disposable bioreactors provide a suitable environment for cell growth while minimizing the cross-contamination risk. The bags are manufactured from multilayer, laminated, clear USP Class VI plastics and are easily connected to the full suite of Xuri Cell Expansion cell culture, purification, and fluid handling products. The selection of Cellbag bioreactors is listed in Table 2. For more information about Cellbag bioreactors, see data file 29-0618-52.

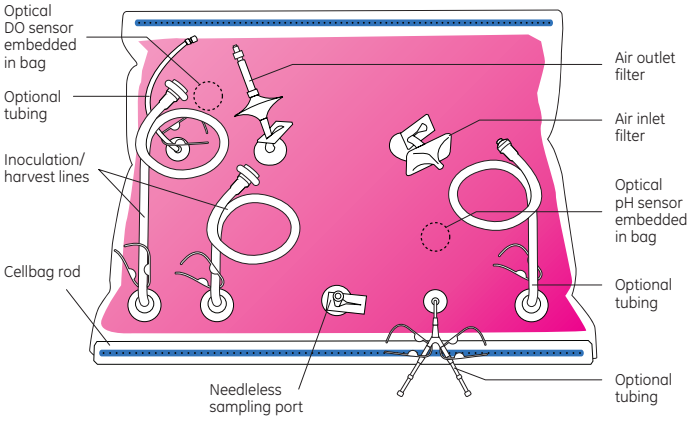

Fig 8. Presentation of typical Cellbag bioreactor fittings.

Table 2. Selection of Cellbag bioreactor sizes

Cellbag bioreactor*	Working volume
Cellbag 2 l	300† ml to 1 l
Cellbag 10 l	500 ml to 5 l
Cellbag 20 l	1 to 10 l
Cellbag 22 l	1 to 10 l
Cellbag 50 l	5 to 25 l

* All Cellbag bioreactor sizes are available with internal perfusion filter for perfusion cultures and/or can be equipped with single use optical pH (pHOPT) and DO (DOOPT II) sensors.

† Cellbag bioreactors with optical sensors require 300 ml minimal working volume. Depending on application and configuration, it might be possible to cultivate below the recommended minimum volume. However, it is highly recommended to stay above this volume for applications that require high agitation and pH and DO control. The temperature, pH, and DO sensors need to be submerged in liquid throughout the complete rocking cycle to function correctly.

System specifications

System specifications are listed in Table 3.

Table 3. Xuri Cell Expansion W25 specifications

General system specifications

Control system	UNICORN 6.3 or later version	
Dimensions, W × H × D		
Base unit	404 × 560 × 205 mm	
Tray 10	475 × 430 × 60 mm	
Tray 20	740 × 480 × 70 mm	
Tray 50	800 × 610 × 70 mm	
Lid 10	475 × 430 × 230 mm	
Lid 20	740 × 480 × 245 mm	
Lid 50	800 × 610 × 260 mm	
Environmental Control Unit	276 × 360 × 117 mm	
Pump 25	275 × 280 × 115 mm	
Weight		
Base unit	24 kg	
Tray 10	4.5 kg	
Tray 20	7.3 kg	
Tray 50	9.5 kg	
Lid 10	1.7 kg	
Lid 20	3.3 kg	
Lid 50	3.9 kg	
Environmental Control Unit	4.8 kg	
Pump 25	3.8 kg	
Power supply	100 to 240 V, ~ 50 to 60 Hz	
Power consumption	1500 VA	
Enclosure protective class	IP 21	
Gas supply	Normal capacity	Fast-fill capacity
External air supply, 1.0 to 1.5 bar	1.3 l/min	3.5 l/min
External CO_2 supply, 1.0 to 1.5 bar	0.2 l/min	0.5 l/min
External O_2 supply, 1.0 to 1.5 bar	0.7 l/min	1.7 l/min

Environmental aspects

Operating ambient temperature range	15°C to 32°C
Operating humidity range	20% to 80% (noncondensing)

Xuri Cell Expansion System W25, base unit

Rocking speed control range[1]	2 to 40 rpm
Rocking angle control range[1]	2° to 12°
Rocking motion control range	15% to 100%
Media weight control range	0.5 to 25 kg
Scale, absolute accuracy	± 0.050 kg + 1% of load kg
Temperature sensor	Pt100 Class A
Temperature measurement range	2°C to 50°C
Temperature control range	20°C (or ambient temperature + 5°C) to 40°C
Temperature control accuracy (incl. measurement error)	± 0.5°C

[1] When cultivating in a 50 l Cellbag bioreactor at maximum working volume of 25 l, rocking speed and angle multiplied should not exceed 240 rpm degrees. For example, if the rocking angle is set to 12 degrees, the rocking speed should not be set higher than 20 rpm.

Xuri Cell Expansion W25 Environmental Control Unit

Gas flow control range	0 to 1000 ml/min
Gas flow total accuracy (process value to reference flow)	± 10 ml/min + 3% of read value
Fast-fill flow	~ 3 l/min
CO_2 control range	0% to 15%
CO_2 measurement accuracy	± 0.3% + 3% of read value when mixed only with air/N_2
Total CO_2 accuracy (process value to reference CO_2 content)	± 0.7% + 3% of read value
O_2 control range	0% to 50% when mixed with N_2, 21% to 50% when mixed with air
O_2 measurement accuracy	± 0.6% + 1% of read value within 0% to 50% when mixed only with air/N_2
Total O_2 accuracy	± 1.2% + 1% of read value
pH measurement range	4.5 to 8.5
pH measurement accuracy	± 0.05 for pH 6.75 to 7.25 ± 0.1 for pH 6.5 to 7.5
pH control range	6.0 to 8.0
Total pH accuracy (process value to reference pH)	± 0.1 for pH 6.75 to 7.25 ± 0.15 for pH 6.5 to 7.5
DO measurement range	0% to 250% air saturation
DO measurement accuracy	± 5% air saturation (excl. atmospheric pressure variations)
DO control range	0% to 100% air saturation
Total DO accuracy (process value to reference DO)	± 10% air saturation (excl. atmospheric pressure variations)

Xuri Cell Expansion W25 Pump

Pump flow rate range	100 ml to 144 l/d (0.07 to 100 ml/min)
Pump flow accuracy	± 0.1 ml/min + 5% of read value after calibration
Accumulated pumped volume accuracy	± 10% of measured volume
Supported tubing dimensions	i.d. 0.5 to 4.8 mm (1/50" to 3/16") wall thickness: 1.6 mm (1/16")

System components

Product	Description
Xuri Cell Expansion System W25 Base Unit	Base unit
Xuri Cell Expansion System W25 Environmental Control Unit pH	Gas flow/mix and pH
Xuri Cell Expansion System W25 Environmental Control Unit Full	Gas flow/mix, pH, and DO
Xuri Cell Expansion System W25 Pump	Pump
UNICORN 6.3.2 WrkStn-pure-BP	Software and license
UNICORN 6.3 Remote License	–
UNICORN 6.3 Dry license	–
Tray 10	–
Tray 20	–
Tray 50	–
Lid 10	–
Lid 20	–
Lid 50	–
Filter heater	–
Bag sensor adaptor 2.5 m assembly	Fiber cable for pH and DO control

Related literature	Code number
UNICORN 6.3 Manual Package	29-0234-67
UNICORN 6 control software, data file	28-9573-46
Validation Support File UNICORN 6.3	11-0029-94

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